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EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,735	MINDEN, JONATHAN SAMUEL	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 24, 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *10-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *November 21, 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges Applicant's reply, filed August 24, 2005. No amendment to the claims was made. Currently, claims 1-9 and 25-29 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The disclosure is objected to because of the following informalities:

> Throughout the Specification, the recitation of "half life" of binding or "half life" of release is indefinite because it is not clear how one skilled in the art can make a capture device having a specific "half-life of binding" or a specific "half life of release" when the definitions of "half-life of binding" and the "half life of release" only take into account the parameter of time (i.e. the amount of time required to covalently bind or release half the protein), and do not take into account initial concentration of reactants as well as the forward and reverse rate constants.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention. Specifically, the specification does not enable one skilled in the art to make a capture device having a specific "half-life of binding" or a specific "half life of release."

Claim 1 recites a biomolecule capture device "having a half-life of binding of desired biomolecules of less than 1 hour; and a half life of release of desired biomolecules of less than 1 hour." The specification defines the term "binding half life" as the amount of time required to covalently bind half the protein in a solution (see Specification at p. 12, lines 5-7). In addition, the specification defines the term "release half life" as the amount of time required to release half of the protein which is covalently bound (see Specification at p. 12, lines 8-10).

The definitions of "binding half life" and "release half life," as recited in the Specification, do not appear to take into account any reaction rate constants or the initial concentration of maleic anhydride biomolecule-binding compound or the initial concentration of biomolecules. For example, the specification does not appear to specify the concentration of "proteins in a solution" in the definition of "binding half life." In addition, the specification does not appear to specify the concentration of "protein which is covalently bound" in the definition of "release half life."

According to Lodish et al., MOLECULAR CELL BIOLOGY, Section 2.3 (2000), the rate of a chemical reaction is affected by the initial concentration of reactants as well as the forward and reverse rate constants (see Equations 2-3, 2-4). Here, since the definitions of "half-life of binding" and the "half life of release" only take into account the parameter of time (i.e. the amount of time required to covalently bind or release half the protein), and do not take into account initial concentration of reactants as well as the forward and

reverse rate constants, it is not clear how one skilled in the art can make a capture device having a specific "half-life of binding" or a specific "half life of release."

In the decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), the factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Here, the state of the prior art does not appear to recognize the concepts of "half-life of binding" or "half life of release" such that a person of ordinary skill would not be apprised of their definitions or the protocol for their determination. In addition, the Specification does not provide direction to a location in the technical literature to educate a person of ordinary skill as to the concepts of "half-life of binding" or "half life of release" and the protocol for their determination. Finally, the Specification does not provide working examples relating to the measurement of "half-life of binding" or "half life of release." Given Applicant's limited description of "half-life of binding" or "half life of release," the quantity of experimentation needed to make a capture device having a specific "half-life of binding" or a specific "half life of release" is undue.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The specific claim rejections under 35 USC 112, second paragraph, set forth infra, may be considered relevant to other claims not explicitly mentioned, as deemed reasonably appropriate.

In claim 1, the recitation of "the maleic anhydride biomolecule-binding compound having a half life of binding of desired biomolecules of less than 1 hour; and a half life of release of desired biomolecules of less than 1 hour" is indefinite because it is not clear how one skilled in the art can make a capture device having a specific "half-life of binding" or a specific "half life of release" when the definitions of "half-life of binding" and the "half life of release" only take into account the parameter of time (i.e. the amount of time required to covalently bind or release half the protein), and do not take into account initial concentration of reactants as well as the forward and reverse rate constants.

In claims 1 and 25, the recitation of "a maleic anhydride biomolecule-binding compound" is grammatically awkward and is indefinite because it is not clear whether "maleic anhydride biomolecule" and "binding compound" are physically separate entities, or whether "maleic anhydride biomolecule" and "binding compound" are a single entity. In claim 1, the recitation of "the maleic anhydride biomolecule-binding compound having a half life of binding of desired biomolecules" is indefinite because it is not clear whether/how "biomolecules" are incorporated into the claimed device. It is not clear whether "biomolecules" is a required claim limitation. The hyphen between "biomolecule" and "binding compound" is indefinite because it is not clear whether the hyphen joins a noun (i.e. "biomolecule") with a noun (i.e. "binding compound"), or whether the hyphen joins a noun (i.e. "biomolecule") with an adjective (i.e. "binding"). In addition, the functional relationship represented by "-" is not clear.

In claim 8, the recitation of "the desired biomolecule" lacks antecedent basis in claim 1. It is not clear whether "biomolecules" is a limitation required in claim 1.

In claims 8-9, the recitation of "amine containing compound" is grammatically awkward and is indefinite because it is not clear whether/how "an amine" is capable of containing a compound. In addition, it is not clear whether said "amine containing compound" references "biomolecule", or whether said "amine containing compound" is a physically separate entity from "biomolecule." In claim 9, it is not clear whether "a protein" references said "amine containing compound" and/or said "biomolecule", or whether "a protein" is a physically separate entity from said "amine containing compound" and/or said "biomolecule."

Claim Rejections - 35 USC § 102

Claims 1-4, 7-9, are rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al., 203 ARCH. BIOCHEM. BIOPHYS. 774 (1980).

Singh et al. describe a biomolecule capture device comprising a substrate (see Title, "Solid Support") and a maleic anhydride biomolecule-binding compound covalently bound to the surface (see Abstract, "MPE-agarose"). The device of Singh et al. is necessarily capable of "having a half-life of binding of desired biomolecules of less than 1 hour; and a half life of release of desired biomolecules of less than 1 hour", and would be so recognized by persons of ordinary skill in the art.

With respect to claims 2-4, 7, 26 and 28-29, Singh et al. describe a biomolecule capture device comprising aminohexyl agarose (see Abstract, "MPE-agarose") solid support.

With respect to claims 8-9, Singh et al. describe a biomolecule capture device comprising a protein containing an amine (see Abstract, "bovine serum albumin").

Claims 1-3, 5-9, 25 and 27-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Johnson et al. (US 6,372,813).

Johnson et al. describe a biomolecule capture device comprising a substrate and a maleic anhydride biomolecule-binding compound covalently bound to the surface (see Fig. 3). The device of Johnson et al. is necessarily capable of "having a half-life of binding of desired biomolecules of less than 1 hour; and a half life of release of desired biomolecules of less than 1 hour", and would be so recognized by persons of ordinary skill in the art.

With respect to claims 2-3 and 28-29, Johnson et al. describe a biomolecule capture device wherein the substrate comprises polyamide (see col. 4, line 59).

With respect to claims 5-6, 25 and 27, Johnson et al. describe a biomolecule capture device comprising dimethyl maleic anhydride (see Fig. 3).

With respect to claims 8-9, Johnson et al. describe a biomolecule capture device comprising a protein containing an amine (see col. 7, lines 45-46).

Claim Rejections - 35 USC § 103

Claim 5-6 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al., 203 ARCH. BIOCHEM. BIOPHYS. 774 (1980), in view of Kinsella & Shetty (US 4,348,479).

Singh et al. describe a biomolecule capture device as substantially described supra. Singh et al. do not describe a device comprising a dialkyl maleic anhydride.

However, Kinsella & Shetty teach the use of dimethyl maleic anhydride (see col. 3, line 43) for capturing biomolecules (see Title, "proteinaceous material"). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the biomolecule capture device of Singh et al. with dialkyl maleic anhydride because Kinsella & Shetty discovered that proteins can be reversibly captured with cyclic anhydrides, including dimethyl maleic anhydride, in as little as 15 minutes (see col. 4, line 26) and released in as little as 20 minutes (see col. 4, line 68).

Response to Arguments

In prior Office Action, claims 1-9 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Specifically, the specification does not enable one skilled in the art to make a capture device having a specific "half-life of binding" or a specific "half life of release." In response, Applicant provides argumentation that appears to be premised on the position that pH is determinative of "half-life of binding" and/or "half life of release" (see Applicant's reply, p. 1, fourth paragraph). In addition, Applicant appears to argue that persons skilled in the art need only rely on well-established techniques, e.g. an assay, to enable Applicant's definition of "half-life of binding" or "half life of release" (see Applicant's reply, paragraph bridging pp. 1-2). Finally, Applicant appears to argue that Shetty & Kinsella, 191 BIOCHEM. J. 269 (1980), enable Applicant's definition of "half-life of binding" and/or "half life of release" (see Applicant's reply, p. 2, first full paragraph). Applicant's arguments have been carefully considered but are not persuasive for the following reasons:

Claim 1 recites a biomolecule capture device comprising, inter alia:

> (b) a maleic anhydride biomolecule-binding compound covalently bound to the surface of the substrate invention, the maleic anhydride biomolecule-binding compound having a half life of binding of desired biomolecules of less than 1 hour; and a half life of release of desired biomolecules of less than 1 hour. (emphasis added)

Applicant's specification defines the term "binding half life" as the amount of time required to covalently bind half the protein in a solution (see Specification at p. 12, lines 5-7). In addition, the specification defines the term "release half life" as the amount of time required to release half of the protein which is covalently bound (see Specification at p. 12, lines 8-10).

In Applicant's reply, filed August 24, 2005, Applicant argues:

> Specifically, the amount of unbound biomolecules present, during either the binding phase (a first pH) or release phase (a second pH), can be easily empirically measured

> using well established techniques apparent to one of skill in the art, e.g., an assay. Accordingly, using the techniques such as an assay, one of skill in the art can very easily determine, with little experimentation using well established techniques, the time duration for half of the biomolecules to bind to (at a first pH) or release from (at a second pH) the apparatus of the presently claimed invention. (emphasis added)

However, Applicant's specification does not disclose a step of measuring the amount of unbound protein at a first and second pH to derive a "binding half life" or "release half life". Applicant's specification does not disclose a step including an assay for measuring the amount of unbound protein at a first and second pH to derive a "binding half life" or "release half life". Applicant's specification does not disclose a step of measuring the time duration for half of the protein to bind to (at a first pH) or release from (at a second pH) the apparatus of the presently claimed invention to derive a "binding half life" or "release half life", respectively.

Applicant's argument premised on the position that pH is determinative of "half-life of binding" and/or "half life of release" (see Applicants' reply, p. 1, fourth paragraph) appears to be in direct conflict to Applicant's explicit definition of "half-life of binding" and/or "half life of release" as set forth in Applicant's specification (see specification, p. 12, first full paragraph):

> Specifically, in certain embodiments of the present invention, the amount of time required to covalently bind half of the proteins in solution is defined herein as the "binding half life." The present invention can reduce the binding half life from hours to minutes. Similarly, in certain embodiments of the present invention, the amount of time required to release half of the protein which is covalently bound to the biomolecule-binding compound is defined herein as the release half life. The present invention can reduce the release half life from hours to minutes. (emphasis added)

Examiner observes that Applicant's explicit definitions of the concepts of "binding half life" and "release half life" include no characterizing parameters other than "amount of time". In addition, Applicant's specification does not appear to set forth an explicit causal relationship between pH and "binding half life", or pH and "release half life". Consequently, even when the claims are interpreted in light of Applicants' specification, it is not clear whether persons skilled in the art would be so imaginative as to import the

clarifying details of Applicant's argumentation into the plain meaning of Applicant's claimed invention to arrive at the concept of "half life", as described in Applicant's reply.

Applicant's argument that persons skilled in the art need only rely on well-established techniques, e.g. an assay, is persuasive in part. Given Applicant's explicit definition of "binding half life" and "release half life", persons skilled in the art would readily conclude that at least a stopwatch is needed to measure "binding half life" and "release half life". However, it is not entirely clear whether persons skilled in the art would have the requisite ability (or patience) to use said stopwatch, for example, to measure the "half life" of reactions with relatively small forward or reverse equilibrium constants, i.e. reactions requiring an indefinite amount of time to satisfy Applicant's definition of "half life". Knowledge of the molecularity of a reaction (e.g., unimolecular, bimolecular, etc.), although interesting, does not appear to be helpful to persons skilled in the art having to wait an indefinite amount of time for a reaction to proceed to Applicant's "half life" endpoint.

Although Applicant posits that "the amount of unbound biomolecules present, during either the binding phase (a first pH) or release phase (a second pH), can be easily empirically measured using well established techniques apparent to one of skill in the art", Examiner posits that Applicant's disclosure does not lead one of skill in the art to do so because Applicant's explicit definitions of the concepts of "binding half life" and "release half life" include no characterizing parameters other than "amount of time" and Applicant's specification does not appear to set forth an explicit causal relationship between pH and "binding half life", or pH and "release half life".

Applicant reliance on the teachings of Shetty & Kinsella, 191 BIOCHEM. J. 269 (1980), to enable Applicant's usage of the terms "half-life of binding" and "half life of release" is not persuasive. Shetty & Kinsella describe an uncontrolled experiment measuring nitrogen in dialyzed, freeze-dried, digested protein samples at pH 9.0. Shetty & Kinsella do not measure a disappearance of citraconylated protein,

or an appearance of citraconylated protein, and thus do not perform measurements of "half life" in accordance with Applicant's explicit definition.

In prior Office Action, claim 1 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "the maleic anhydride biomolecule-binding compound having a half life of binding of desired biomolecules of less than 1 hour; and a half life of release of desired biomolecules of less than 1 hour". In response, Applicant argues that "one of skill in the art can easily determine the specific half life of binding or release for a device of the present invention" (see Applicant's reply, p. 2, last full paragraph). Applicant's argument is not persuasive for the reasons set forth supra.

In prior Office Action, claims 1 and 25 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "the maleic anhydride biomolecule-binding compound having a half life of binding of desired biomolecules". In response, Applicant appears to argue that "biomolecules" are necessary to measure "half life" (see Applicant's reply, paragraph bridging pp. 2-3). In addition, Applicant argues that the phrase "a maleic anhydride biomolecule-binding compound" refers to a single entity (see Applicant's reply, p. 3, second and third full paragraphs). Applicant's arguments are not persuasive because it is not clear from Applicant's argumentation how "biomolecules" are necessary when "a maleic anhydride biomolecule-binding compound" refers to a single entity.

In prior Office Action, claims 8-9 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "amine containing compound". In response, Applicant argues that an "amine containing compound" ≈ "compound that contains an amine". Applicant's argument is not persuasive because the scope of the two phrases are not equivalent, the later phrase being more concise and consistent with Applicant's specification.

In prior Office Action, claims 1-4, 7-9, were rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al., 203 ARCH. BIOCHEM. BIOPHYS. 774 (1980). Claim 5-6 and 25-29 were rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al., 203 ARCH. BIOCHEM. BIOPHYS. 774 (1980), in view of Kinsella & Shetty (US 4,348,479). Finally, claims 1-3, 5-9, 25 and 27-29 were rejected under 35 U.S.C. 102(e) as being anticipated by Johnson et al. (US 6,372,813). In response, Applicants argue that neither Singh et al. (see Applicants' reply, p. 3, last paragraph) nor Johnson et al. (see Applicants' reply, p. 4, third paragraph) describe a maleic anhydride compound. Applicants' argument has been carefully considered but is not persuasive because Applicants' invention, as claimed, may not require a maleic anhydride compound. Independent claims 1 and 25 merely require a "maleic anhydride biomolecule-binding compound". The phrase "maleic anhydride biomolecule-binding compound" may simply require a compound effective for, or capable of, binding maleic anhydride biomolecules. This interpretation has support in Applicants' specification, which also describes a compound (see specification, p. 10, lines 9-12, "protein from a solution") effective for, or capable of, binding maleic anhydride biomolecules (see specification p. 10, lines 13-14, "maleic anhydride bound to a substrate"; p. 5, line 19, "[t]he substrate can be... collagen"). Similarly, Singh et al. appear to describe a maleic anhydride biomolecule-binding compound (see Abstract, "MPE-agarose") that is effective for, or capable of, binding maleic anhydride biomolecules. Thus, the limitations of Applicant's claimed invention are fully met.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
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djv

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09/30/05